Journal of Clinical Virology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Review

Epidemiology and impact of HIV coinfection with Hepatitis B and Hepatitis C viruses in Sub-Saharan Africa

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ARTICLE INFO

Article history:
Received 9 February 2014
Received in revised form 22 May 2014
Accepted 29 May 2014

Keywords:
HIV-1
Hepatitis B
Hepatitis C
Coinfection
Africa
Epidemiology

ABSTRACT

Human immunodeficiency virus (HIV), Hepatitis B (HBV) and Hepatitis C (HCV) are blood-borne viruses with shared routes of transmission. In high-income settings, the impact of antiretroviral therapy (ART) on survival has unmasked chronic liver disease from viral hepatitis B or hepatitis C as a leading cause of morbidity and mortality in individuals with HIV infection. It is now feared that progressive liver disease may threaten the success of ART programmes in developing countries, where HCV or HBV testing and monitoring are not yet systematic among HIV-infected patients and ART use is generally blind to these co-infections. We set out to review recent data from Sub-Saharan Africa, in order to build a detailed and up-to-date picture of the epidemiology and emerging impact of HBV and HCV coinfection in countries at the heart of the HIV pandemic. There is a preponderance of HIV/HBV coinfection compared to HIV/HCV in this region, and significant caveats exist regarding the accuracy of published HCV seroprevalence surveys. Morbidity and mortality of coinfection is significant, and may be further enhanced in African populations due to the influence of host, viral and environmental factors. Careful scrutiny of the coinfection problem is vital to inform an approach to directing resources, planning public health initiatives, providing clinical care, and guiding future research.

Contents

Abbreviations: 3TC, Lamivudine; ALT, alanine transaminase; Anti-HBcAb, antibody to Hepatitis B core antigen; Anti-HBeAb, antibody to Hepatitis B e-antigen; Chronic hepatitis B, persistence of HBsAg >6months; d4T, Stavudine; ddI, Didanosine; DAA, Direct Acting Antivirals; HAART, Highly Active Anti-Retroviral Therapy; HBcAb, Hepatitis B core antibody; HBeAg, Hepatitis B e-antigen; HBsAg, Hepatitis B surface antigen; HBV, Hepatitis B virus; HBV DNA, Hepatitis B virus DNA; HCC, hepatocellular carcinoma; HCV, Hepatitis C virus; HCV-Ab, Hepatitis C antibody; HIV, human immunodeficiency virus (type 1); PEG-IFN, pegylated-interferon-α; RBV, ribavirin; TDF, tenofovir; WHO, World Health Organisation.

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http://dx.doi.org/10.1016/j.jcv.2014.05.018
1386-6532/

1. Introduction

In the past two decades, there has been a progressive decrease in mortality from AIDS-related opportunistic infection and malignancy, due to the success of ART. However, this has left a niche for the emergence of liver pathology as a leading cause of morbidity and mortality in HIV patients coinfected with HBV or HCV [1,2]. Most characteristically, HIV promotes chronicity, liver fibrosis and malignancy in both HBV and HCV infection [3–7]. Conversely, the hepatitis viruses have been recognized for their potential association with worse HIV outcomes [1,8–11], although this is by no means universal [12].

Antiviral therapy can be difficult in the context of coinfection, as HIV-infected individuals characteristically respond less well to treatment for HBV or HCV, and are at increased risk of hepatotoxicity and drug interactions [7,13,14]. The overlapping antiviral spectrum of therapy for HIV and HBV can also cause complexities due to the enhanced potential for selection of drug-resistance mutations [4,15,16].

HIV/HBV coinfection represents a particular challenge in Africa: over two-thirds of the global total of 34 million people with HIV are in Sub-Saharan Africa [17], corresponding to regions of high HBV endemicity (Table 1; Figs. 1 and 2) [10,18,19]. With HCV, there is a paucity of seroprevalence estimates from Africa, making it difficult to quantify the true burden of chronic carriage or to identify clear risk factors for infection. There are further complications in assessing and managing disease in Africa, including limited data availability, and a variety of host, viral and environmental factors that contribute to morbidity of co-infection (Fig. 3).

In contrast to the high profile afforded to HIV, chronic hepatitis infections have frequently been under-resourced, with poor investments in education, clinical awareness and public health [20,21]. Decision-making and care provision in African settings may be further hampered by the lack of epidemiological data [18,22–24], the significant burden of morbidity, the associated therapeutic challenges, and the need for increased political and public profiles have led to recent expert calls for urgent attention to the coinfection problem [3,20,21].

We have therefore set out to review the interplay between HIV, HBV and HCV, considering specifically the epidemiology and clinical impact of coinfection, and focusing particularly on the overlapping epicentres of hyperendemic HIV/AIDS and HBV populations in Sub-Saharan Africa.

2. Methods

We searched PubMed and the Global Health Library via the African Index Medicus, using the terms "HIV", and "Africa", together with "coinfection", "hepatitis", "HBV" or "HCV", and "epidemiology", "virology", "complications" and "hepatocellular carcinoma", including references in English and French. We also included relevant guidelines, review articles, and additional citations from papers identified by our literature search.

We prioritized literature from the past decade (published ≥2004), and elected to focus specifically on Sub-Saharan Africa, as this differs from Northern Africa (in particular from the unique circumstances of Egypt). Selected references from cohorts elsewhere in the world were included if deemed to contribute significantly to informing our understanding.

3. Epidemiology of coinfection

Although HIV, HBV and HCV are blood-borne viruses, predominant mechanisms and timing of infection differ, leading to variable patterns of epidemiology.

In most Sub-Saharan regions, HIV/HBV coinfections substantially out-number HIV/HCV (Tables 2 and 3; Fig. 4) [12,14,25–30]: in the studies reviewed here, chronic HBV coinfection was reported in up to 36% of all HIV-positive subjects, with the highest rates in West Africa, and certain Southern African cohorts (Table 2). HCV coinfection is less common (Table 3), reflecting low prevalence of injecting drug use (IDU) [22,27,31]. Although higher HCV seroprevalence has been reported in some cohorts [63,64], these figures depend upon the method of ascertainment, and may be over-estimated if HCV Ab alone was used for screening.

In Africa, HBV infections acquired in early childhood contribute substantially to the overall burden of disease [32–34]. The precise

Table 1
Epidemiology of HIV, HBV and HCV.

	HIV	HBV	HCV
Total number of people infected worldwide (percentage of these in Subsaharan Africa); also see Fig. 2	34 million [17] (70%)	350–400 million [32,139] (15%)	130–170 million [32,139,140] (20%)
Chronicity following acute infection	~100%	90% if infected in infancy 10% if infected in adulthood	80% (increased risk of progressive disease in older adults)
Distribution/ prevalence in Africa	Epicentre in Southern Africa, with e.g. 20% population prevalence	High endemicity in most of Southern Africa [42]; (≥8% population prevalence HBsAg)	Variable by region: E.g.15-25% in Egypt [36,140]; 1–2% in Southern Africa
Number of deaths/year (worldwide)	1.8 million [17]	600,000 [141]	>350,000 [140]
Number of individuals with co-infection[a]	HBV: 2–4 million [3,32] HCV: Estimates vary from 4–5 million [32] up to 10–15 million [89]	HCV:10–20% [142]	HBV: 2–20% [142]

[a] Co-infection rates are estimates only; true numbers are not possible to ascertain, as there are substantial differences between regions, many populations are not well characterized and data may be confounded by false negative results (E.g. occult HBV infection).

Please cite this article in press as: Matthews PC, et al. Epidemiology and impact of HIV coinfection with Hepatitis B and Hepatitis C viruses in Sub-Saharan Africa. J Clin Virol (2014), http://dx.doi.org/10.1016/j.jcv.2014.05.018